

Multiple hypertrophic relapsing remitting cranial neuropathies as an initial presentation of primary CNS lymphoma without any brain or spinal cord lesion

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Abstract

Cranial nerve thickening as an initial isolated presentation of CNS lymphoma is rare. Once an extremely rare neoplasm, primary lymphoma of the central nervous system (CNS) now ranks only next to meningiomas and low-grade astrocytomas in prevalence. Multiple cranial nerve thickening can be a feature of primary CNS lymphoma. Here we report a case of a 45-year-old immunocompetent female who presented with relapsing remitting multiple cranial nerve thickening as an initial feature of primary CNS lymphoma without any other brain or spinal cord lesions.

Key words: Cisternal segments; lymphoma; multiple cranial nerve thickening; primary CNS lymphoma

Introduction

Primary CNS lymphoma (PCNSL) accounts for 1-5% of all brain tumors^[1,2] and approximately 1% of all Non-Hodgkin Lymphoma NHL. The incidence rates of PCNSL are increasing among immunocompetent patients.^[1,3,4] Immunocompromised patients (e.g., individuals infected with HIV) have an increased risk of developing PCNSL.^[5]

The frequency of secondary CNS lymphoma (SCNSL) in patients with systemic lymphoma varies and is highly dependent on the histologic subtype. Patients with

extranodal involvement and those with primary or acquired immunodeficiency disorders carry an increased risk of CNS relapse.^[6]

Early diagnosis of CNS lymphoma is crucial for proper management in both immunocompetent and immunocompromised individuals and is more likely if a tumor is observed on imaging.^[7-9] Although CNS lymphomas may have characteristic imaging findings on traditional CT and MR imaging, none of these will unequivocally differentiate CNS lymphoma from other brain lesions.^[6,9-11] A visible tumor on imaging is essential to raise the suspicion of CNS lymphoma, which can then lead to an early histologic diagnosis based on cytology of the cerebrospinal fluid (CSF) or brain biopsy.

Case Report

A 45-year-old immunocompetent female presented with complaints of headache since 3 months and left ptosis and diplopia since 2½ months. Her headaches were gradual

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in onset, occurring initially in the left frontal region but subsequently progressing to involve the peri-orbital and occipital regions. After about 10 days, the patient also noted drooping of left eyelid and subsequently developed diplopia in all gazes. Patient also mentioned numbness of left half of the face and deviation of angle of mouth to the right. There was no history of fever or neck pain/stiffness. Past medical history was only significant for hypertension.

On cranial nerve examination, the positive findings were dilated left pupil with absent direct and indirect light reflex, left third and partial sixth nerve paresis, impaired sensations of left face and forehead, absent left corneal reflex, and bilateral facial weakness. Rest of the sensory and motor examination was normal. Plantar reflex was negative and tandem gait was impaired.

Contrast CT brain was done and revealed homogeneously enhancing bilateral trigeminal, left oculomotor right facial and vestibulocochlear nerves [Figure 1]. Subsequent evaluation with contrast magnetic resonance imaging (MRI) brain showed diffusely thickened cisternal segments of left oculomotor, left abducens, bilateral trigeminal, right facial, right vestibulocochlear, glossopharyngeal, vagus, and spinal accessory nerves. Cavernous segment of the left oculomotor nerve was also thickened. On post contrast study, these thickened nerves showed homogenous enhancement. MRI cervical spine screening was done which showed thickening and enhancement of right cervical C6 and C7 spinal nerve roots [Figure 2]. Differential diagnosis given on MRI included leptomeningeal metastases, lymphoma, neurosarcoidosis, and chronic inflammatory demyelinating polyneuropathy (CIDP).

CSF examination was done and revealed no atypical/malignant cells in the CSF. CSF gram stain and Acid-fast bacilli AFB stains were normal. CSF culture was negative. Serum angiotensin-converting enzyme (ACE) and



Figure 1 (A and B): (A and B) Axial post contrast CT images at the level of brainstem show thickened and enhancing cisternal segment of left oculomotor (white arrow) and bilateral trigeminal nerves (black arrows)

serum calcium levels were normal. Screening for HIV and venereal disease research laboratory (VDRL) test turned out to be negative. Contrast CT scan of skull, chest, abdomen, and pelvis was done to rule out any malignancy. However, there was no primary neoplasm detected. Patient was started on Prednisolone 60 mg empirically as the condition was thought to be immune mediated. But the patient's neurological status worsened in the form of bilateral facial nerve palsy and dysphagia. For better immunosuppression, IV methylprednisolone was given for 5 days which resulted in partial recovery of facial paresis and dysphagia. On maintenance prednisolone of 60 mg, the patient complained of intermittent headaches which relieved partially on taking analgesics. Patient was empirically put on four-drug anti-tubercular therapy. Since the patient's condition was worsening clinically, other immunosuppressive agents were started (1 g cyclophosphamide with MESNA). Following immunosuppression with cyclophosphamide, patient's headache decreased to some extent, thus reducing the need to take analgesics. In view of improvement of symptoms, patient was discharged to follow-up after 1 month for the next cycle of cyclophosphamide.

Ten days later, the patient was readmitted with complaints of episodic severe right upper limb pain and dysphagia, intermittent headache, imbalance while walking, decreased hearing bilaterally, intermittent tinnitus, and decreased facial sensations bilaterally. On cranial nerve examination, bilateral oculomotor, trigeminal, facial, and vestibulocochlear nerves were affected suggesting involvement of additional nerves.

Positron emission tomography (PET) imaging was done to rule out metastatic cranial nerve involvement due to an unknown primary; however, it was negative for any primary neoplasm [Figure 3].

In view of worsening of symptoms and new cranial nerve involvement, patient was subjected to left trigeminal nerve biopsy with left side retromastoid suboccipital approach.

Histopathology and immunohistochemistry reports were suggestive of PCNSL-diffuse large B cell lymphoma, CD20 positive [Figure 4].

Discussion

PCNSL presenting as multiple cranial nerve thickening is a rare clinical entity. It has imaging presentation typically in the form of white matter or basal ganglia lesions in contact with CSF surface. These may present as hyperdense areas/masses with variable enhancement on nonenhanced CT (NECT) scans, and as areas of altered signal intensity on MRI with solid enhancement (immunocompetent) or ring enhancement (immunocompromised) with/without areas of hemorrhage/necrosis.^[12]

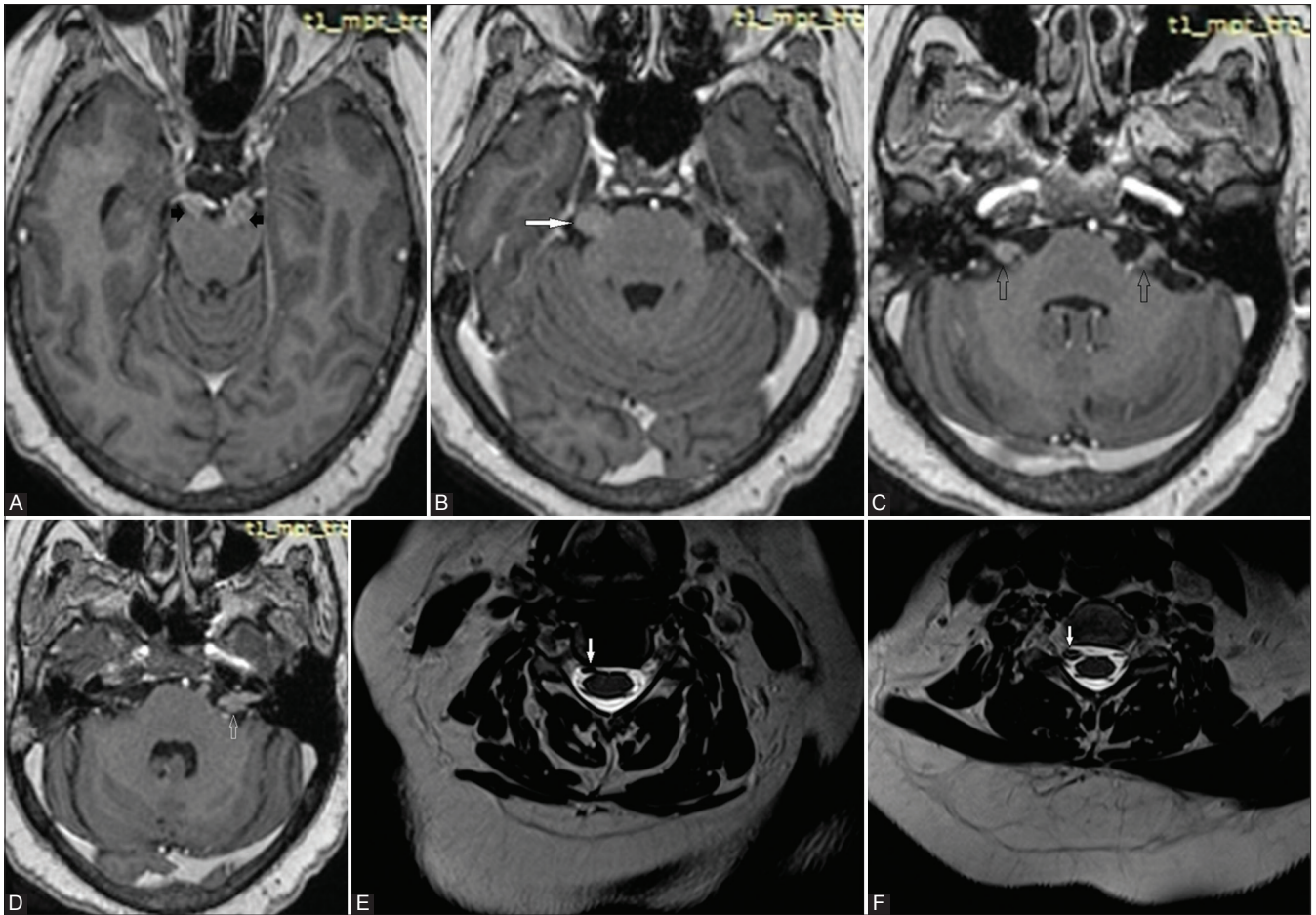


Figure 2 (A-F): (A-D) MRI shows diffuse thickening and enhancement of the cisternal segments of both oculomotor (black arrows), trigeminal (white arrows), and vestibulocochlear and facial nerves (open black arrows). There is also thickening of left abducens, and bilateral glossopharyngeal, vagus, and accessory nerves (open white arrow). (E and F) Thickening of C6 and C7 anterior spinal nerve roots (white arrows)

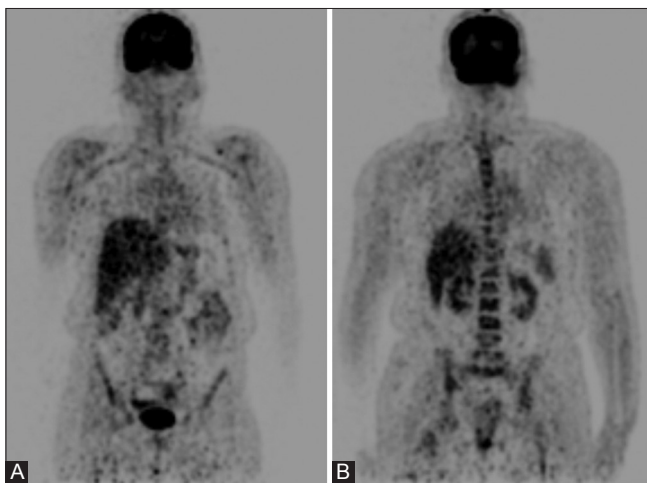


Figure 3 (A and B): (A and B) PET scan images show absence of uptake elsewhere in the body, ruling out the possibility of metastatic cranial neuropathy

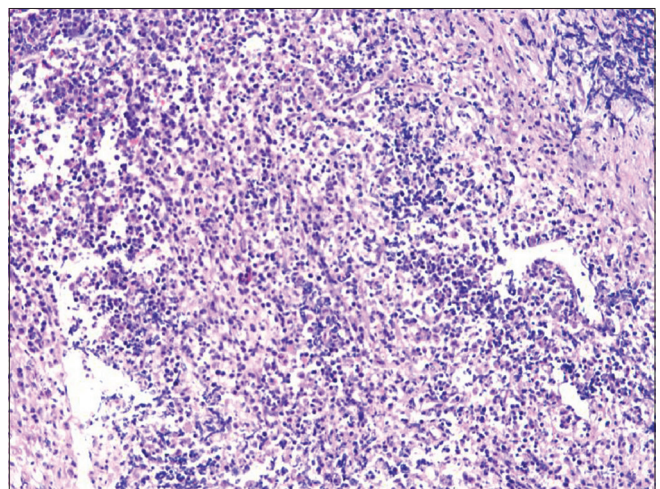


Figure 4: Low power microscopy (×10) image showing diffuse proliferation of small round lymphoid cells having monotonous appearance with few intermediate to large cells infiltrating neural tissue

The SCNSL, by definition, has systemic disease at the time of presentation and more commonly involves leptomeninges with imaging features of leptomeningeal, dural, subependymal, and cranial nerve enhancement.^[13]

In our case, there was predilection for involvement of cisternal segments of the cranial nerves without any intraparenchymal disease (as for PCNSL) and without any systemic involvement (as for SCNSL), which made it a very rare and unusual case.

Our search of literature revealed only one case of lymphoma with isolated cranial nerve involvement, which was a T-cell lymphoma.^[14] This was a case of a 57-year-old male with a histologically proven subcutaneous peripheral T-cell lymphoma. Post chemotherapy, there was relapse and he developed diplopia, dysarthria, and dysphagia. Abnormal lymphoid cells were found in the CSF. Cranial MRI showed thickening of multiple cranial nerves with homogenous enhancement without any parenchymal lesion. This case was different from our case in that our case did not have any extracranial primary lesion. Our search of literature did not reveal specific involvement of cisternal segment of multiple nerves by an intracranial pathology.

The differential diagnosis of cranial nerve hypertrophy, with or without enhancement, includes disorders such as neurosarcoidosis, neoplastic disease (metastatic disease and lymphoma), amyloid neuropathy, neurosyphilis, acute and chronic inflammatory demyelinating polyneuropathy (Guillain–Barré syndrome and CIDP, respectively), other forms of HMSN, and neurofibromatosis type 1 (NF-1). The degree of cranial nerve enhancement, smooth versus irregular nerve enlargement, and the presence or absence of associated leptomeningeal disease may help in narrowing the differential.^[15]

The neuroimaging findings of primary leptomeningeal lymphoma are often unremarkable or may show nonspecific findings such as hydrocephalus. Occasional significant imaging findings may include widespread meningeal calcification, discrete masses or densities, and faint meningeal enhancement. In systemic lymphoma, the intraparenchymal lesions in the brain, when present, typically result from secondary involvement from the leptomeninges via infiltration of the perivascular spaces.^[16]

In neurosarcoidosis, there will be leptomeningeal and pachymeningeal enhancement and also pituitary and hypothalamic involvement along with cranial nerve involvement. The leptomeningeal enhancement (seen in 40% of cases) will be focal or generalized, and will be particularly seen around the basal aspects of the brain and circle of Willis.^[17]

The leptomeningeal metastases from brain primaries like glioblastoma multiforme, anaplastic astrocytoma, ependymoma, and germinoma or from extracranial primaries like breast, lung, and melanoma will lead to leptomeningeal enhancement in a “sugar coated” manner.^[18]

The most common site of enhancement in Guillain–Barré syndrome is considered to be anterior nerve roots. The facial nerve is the most commonly affected cranial nerve in Guillain–Barré syndrome.^[19]

Conclusion

In conclusion, list of differential diagnosis of isolated cranial nerve thickening should include PCNSL along with CIDP (Guillain–Barré syndrome and CIDP, respectively), other forms of HMSN, NF-1, neurosarcoidosis, amyloid neuropathy, and neurosyphilis. Early diagnosis and treatment of this rare manifestation of increasingly common diagnosis of PCNSL in recent years may improve the clinical outcome. Also, MRI remains the modality of choice for the primary diagnosis and follow-up of the cranial nerve pathologies.

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